

**Remarks/Arguments:**

**Status of the Claims**

Claims 25, 27, 29, 31 and 34-37 are in the application.

According to the Official Action Summary, claims 25, 27, 29, 31 and 34-37 have been rejected. However, the Detailed Action does not set forth specific grounds for rejection of claims 25, 27, 34 and 35 other than stating that claims 34 and 35 will be objected to if claims 25 and 27 are found allowable. In the previous Official Action, claims 25 and 27 were deemed allowed.

By way of this amendment, claims 25, 29, 35 and 37 have been amended.

Upon entry of this amendment, claims 25, 27, 29, 31 and 34-37 will be pending.

Applicants respectfully request reconsideration of the pending claims.

**Summary of the Amendment**

The specification has been amended to delete a paragraph originally included in the "Cross Section to Related Applications" and insert it into the "Background of the Invention" section. This paragraph contains a list of U.S. Patents and a U.S. Patent Application, which have been incorporated by reference into the instant application. These U.S. patent documents disclose technology useful in the diagnosis and treatment of cancer. No claim of priority has been made to these patent documents, nor is any such claim intended. Accordingly, the paragraph has been relocated to a more appropriate section of the specification.

Claims 25 and 29 have been amended to make them more clear. As amended, claims 25 and 29 clearly indicate that the claimed method is directed to determining if the individual has cancer. The claims as amended are fully supported by the specification, such as on pages 13 and 14. No new matter has been added.

Claims 35 and 37 have been amended to make them dependent on the presently pending claims, as claims 35 and 37 were dependent on canceled claims due to typographical errors made during preparation of the instant application. As amended, claims 35 and 37 are dependent upon

claims 34 and 36, respectively. The claims as amended are fully supported by the specification. No new matter has been added.

### **Priority**

As noted above, no priority claim has been made to the U.S. patent documents listed in the “Cross Section to Related Applications” section. The paragraph that included the list has been deleted from the “Cross Section to Related Applications” and inserted into the “Background of the Invention” section. The issues regarding priority raised in the Official Action are obviated.

### **Claim Rejections – 35 USC §112**

Claims 29, 31, 36 and 37 stand rejected under 35 USC §112, first paragraph, as containing subject matter which was allegedly not described in such a way to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants respectfully disagree. Applicants respectfully urge that the Examiner has failed to present evidence sufficient to establish that one skilled in the art would doubt the objective truth of Applicants’ assertion of the enablement of the claimed invention. Moreover, Applicants have submitted evidence sufficient to demonstrate that CDX2 is expressed by esophageal cancer cells, and is not expressed by normal esophageal cell.

### **Summary of Position Stated in the Official Action**

Claims 29 and 31 are drawn to methods of diagnosing esophageal cancer; claims 36 and 37 are drawn to methods of confirming the diagnosis of esophageal cancer in individuals who have been previously diagnosed as having the disease. It is noteworthy that there is no discussion in the Official Action related to the Declaration of the inventor, Scott Waldman, filed with Applicants’ Request for Continued Examination Transmittal filed October 2, 2003 pursuant to 37 CFR 1.132, which contains data and other evidence supporting enablement of the present claims.

It is asserted in the Official Action that the claims are rejected

because neither the instant specification nor the current state of the art provides any evidence that the assertion at page 11 lines 13-18

which says that CDX2 is expressed in esophageal cancer cells but not in normal esophageal cells.

The Official Action misquotes Applicants' statement in Amendment Paper No. 12 dated August 19, 2002. Applicants did not state that "CDX2 expression as a cancer biomarker is unpredictable." The Examiner has parsed what Applicant did say, thereby destroying context and leading to a misquote which is completely inconsistent with Applicants' actual stated position. In the Amendment, Applicants were commenting on the Examiner's reliance on Mallo to support the enablement rejection and pointing out that the data referring to the use of colorectal cancer did not support the rejection of claims directed to using CDX2 as a marker for esophageal cancer. Accordingly, Applicants urged that the examiner failed to provide evidence sufficient to establish doubt as to the objective truth of Applicants' assertion of enablement.

In the Official Action, the examiner states:

In order to use the instant invention, undue experimentation involving large numbers of clinical samples is required to assess if CDX2 could also be used as a biomarker for esophageal cancer. It is well known in the art that prior to successful application of newly described markers, research must validate against acknowledged disease end points using histology and/or cytology, establish quantitative criteria for marker presence/absence, and confirm marker value in prospective population trials.

Applicants respectfully urge that no evidence has been provided to support the standard for establishing enablement set forth by the Examiner. The imposition of such standards is without support. The rejection of the claims is therefore contrary to the well established law of enablement.

### **Enablement Law**

It is well established that the requirements of §112, first paragraph, are met so long as: (1) the invention is described in the specification as broadly as it is claimed; and (2) the information provided in the specification is sufficient for persons of ordinary skill in the art having the specification before them to make and use the invention. Moreover, it is well established that in determining whether or not the specification enables the claimed invention, the Patent Office must

accept the objective truth of an Applicant's assertion unless there is some basis to doubt the objective truth of the assertions.

In determining whether or not a disclosure is enabled, Applicants refer to *In re Marzocchi*, 439 F.2d. 220, 223, 169 USPQ 367, 369 (CCPA 1971) which states:

As a matter of Patent Office practice, when a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or cogent scientific reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

### **No Evidence Supporting Rejection**

There has been no such evidence or reasoning substantiating the doubts expressed by the Examiner. As discussed above, Mallo is not relevant to support the rejection of the claimed invention. Moreover, no other evidence is provided, including evidence to support the requirements to establish enablement set forth in the Official Action. There are, in fact, no such requirements and the claims are in compliance with the enablement requirement when the proper analysis to determine enablement is followed.

### **Declaration of Scott Waldman**

As noted above, Applicants have submitted evidence, in the form of a Declaration of Scott Waldman, sufficient to demonstrate that CDX2 is expressed by esophageal cancer cells and not expressed by normal esophageal cell. A duplicate copy of this Declaration is attached hereto for the convenience of the Examiner. The data in the Declaration clearly establish that CDX2 gene transcription product is present in detectable quantities in samples of esophageal cancer but not in normal esophageal tissue samples. In addition, the declaration refers to a publication, Eda, A et al..

*J. Gastroenterol.* (2003) 38(1):14-22, which contains data showing that CDX2 is not expressed in normal esophagus. These data provide evidence sufficient to establish the enablement of the claimed invention.

### **Claims are enabled**

The claims are enabled. Applicants respectfully urge that no valid evidence or cogent scientific reasoning has been provided to question the enablement of the claimed invention. Accordingly, the rejection is improper. Regardless, Applicants have submitted evidence which establishes that the claimed invention is in compliance with the enablement requirement. Accordingly, Applicants respectfully request that the rejection of claims 29, 31, 36 and 37 under 35 U.S.C. §112, first paragraph, be withdrawn.

### **Double Patenting Rejection**

It is stated in the Official Action that should claims 25 and 27 be found allowable, an objection will be made to claims 34 and 35 as being substantial duplicates of claims 25 and 27. As noted above, the Detailed Action sets forth no grounds for rejection of claims 25 and 27 which were deemed allowed in the Official Action dated November 4, 2002. It appears the present Official Action contains an error and that claims 25 and 27 are allowed and an objection is made to claims 34 and 35 as being substantially duplicative to them.

It is asserted by the Examiner that claims 25 and 34 and claims 27 and 35 are duplicates or so close as to cover the same thing despite a slight difference in wording. It is asserted that both claim sets (claims 25 and 27 and claims 34 and 35) appear to obtain tissue samples from patients previously diagnosed with cancer: claim 25, which reads “diagnosing an individual who has stomach cancer,” versus claim 34, which reads “confirming the diagnosis of stomach cancer in an individual who has been diagnosed as having stomach cancer.”

These two claims sets are not identical. The language of claim 25 as set forth above does not require that the individual have been already diagnosed, only that they have stomach cancer. Claim 25 has been amended to clarify this point. As amended, claim 25 now indicates that the method is a method of determining whether or not an individual has stomach cancer. Applicants believe this

Appln. No.: 09/819,252  
Response to Office Action dated January 2, 2004

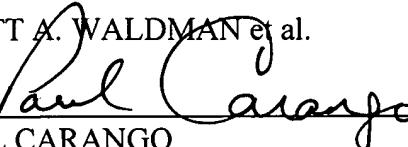
change in language clearly distinguishes the subject matter in claim 25 and 27 to that in claims 34 and 35.

### Conclusion

Claims 25, 27, 29, 31 and 34-37 are in condition for allowance. A notice of allowance is earnestly solicited.

Respectfully submitted,

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Dated:

Attachments: Copy of the Declaration of Scott Waldman